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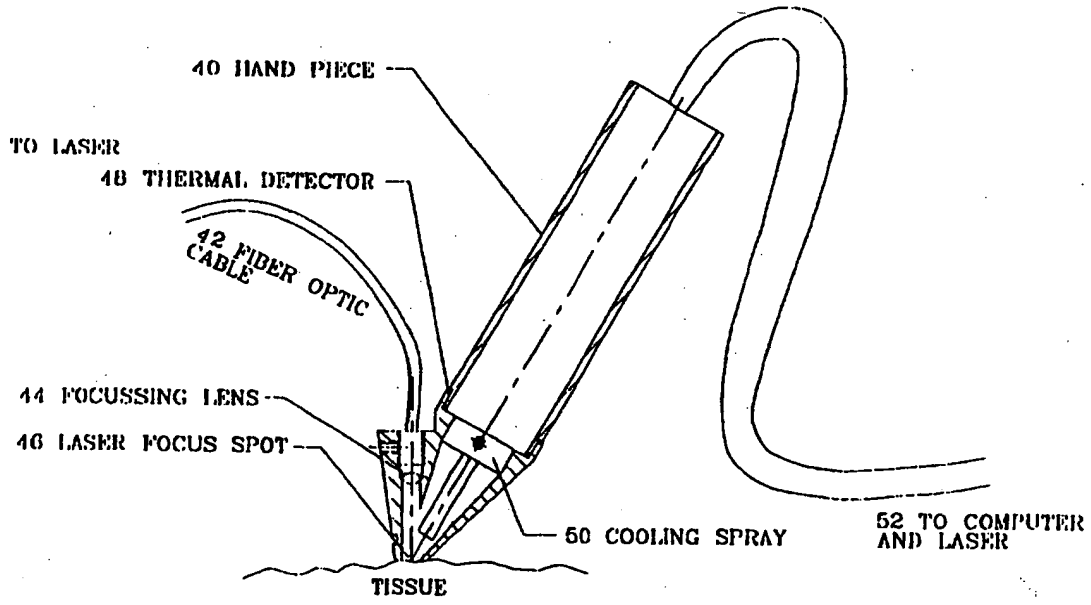

(57) Abstract

An improved method and device for shrinking collagen. In a preferred embodiment, collagen connective tissue in skin is contracted or shrunk, sometimes instantaneously, thus tightening the overlying tissue without the superficial damage or destruction associated with other techniques of superficial skin resurfacing. In another preferred embodiment, the method and device is critical in therapeutic contraction of the collagen connective tissue within the musculo-skeletal system. These techniques match the thickness of the target tissue with the extincting depth or the spectral absorption coefficient of the specific laser wave length to gently heat the collagen molecule to the thermal shrinkage temperature, thus resulting in shrinkage of the underlying tissue while tightening the overlying skin. Superficial heat exchange either by means of passive, or more effectively, by means of a dynamic cooling process enhance this modality by eliminating pain or discomfort and reducing any risk of superficial destruction of the skin.

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Title: IMPROVED METHOD AND DEVICE FOR LASER INDUCED SHRINKING OF COLLAGEN

FIELD OF THE INVENTION

This invention relates to an improved method and device for laser induced shrinking of collagen in humans and other animals. A preferred embodiment of this novel method is directed to the shrinking of collagen in the skin for removing wrinkles and other aesthetic and medical applications, without causing superficial skin damage. Another preferred embodiment of this novel method is directed to the therapeutic contraction of the collagen connective tissue within the musculoskeletal system.

BACKGROUND OF THE INVENTION

The use of lasers for cosmetic surgery by dermatologists and plastic surgeons is expanding rapidly. Despite the fact that reimbursement for these procedures is often not covered under third-party payor health plans, other socio-economic factors seem to be driving the increased demand for these services. Such procedures include laser dosimetry to safely treat and remove vascular lesions (port wine stain and other red marks), benign pigmented lesions (brown marks) and in some cases, tattoo markings from skin surfaces. These procedures, though recently developed, are highly controllable and well known.

Collagen is the single most abundant animal protein in mammals, accounting for up to 30%

of all proteins. The collagen molecule, after being secreted by the fibroblast cell, assembles into characteristic fibers responsible for the functional integrity of tissues making up most organs in the body. The skin is the largest organ of the body occupying the greatest surface area within the human body. As age advances and as a result of other noxious stimuli, such as the increased concentration of the ultraviolet part of the electromagnetic spectrum as radiated from the sun, structural integrity and elasticity of skin diminishes.

Crosslinks between adjacent molecules are a prerequisite for this integrity of the collagen fibers to withstand the physical stresses to which they are exposed. A variety of human conditions, normal and pathological, involve the ability of tissues to repair and regenerate their collagenous framework. In the human, 13 collagen types have been identified. Of the different identifiable types, type I is the most abundant in skin where it makes up 80 to 90 % of the total collagen connective tissue. This type of collagen, however, is less dynamic in the full-grown individual than its counterparts in which collagen is involved in active remodeling. In this case the normal collagen synthesizing activities in skin is relatively quiescent exhibiting slow, almost negligible, turnover.

The extra-cellular matrix of the various connective tissues, such as skin, consists of complex macromolecules, collagen, elastin and glycosaminoglycans (GAGs). The biosynthesis of these macromolecules involves several specific reactions that are often under stringent enzymatic control. The net accumulation of connective tissues is thus, dependent upon the precise balance between the synthesis and the degradation of the connective tissue components.

Previous disclosures, such as U.S. Patents No. 4,976,799 and No. 5,137,539 have described methods and apparatus for achieving controlled shrinkage of collagen tissue. These prior inventions have applications to collagen shrinkage in many parts of the body and describe specific references to the cosmetic and therapeutic contraction of collagen connective tissue within the skin. In the early 1980's it was found that by matching appropriate laser exposure parameters with these conditions, one had a novel process for the nondestructive thermal modification of collagen connective tissue within the human body to provide beneficial changes. The first clinical application

of the process was for the non-destructive modification of the radius of curvature of the cornea of the eye to correct refractive errors, such as myopia, hyperopia, astigmatism and presbyopia. New studies of this process for the previously unobtainable tightening of the tympanic membrane or ear drum for one type of deafness have been made.

In addition to addressing the traditional method of collagen shrinkage wherein the ambient temperature is elevated within the target tissue by about 23 degrees Celsius, the "thermal shrinkage temperature" of collagen, T_s, a novel method for obtaining controlled contraction of collagen at a much lower temperature has been developed. Evidence exists to elevate the mechanical role played by the GAGs in the collagenous matrix. Removing or altering these interstitial chemicals by enzymes or other reagents as disclosed in U.S. Patent No. 5,304,169 considerably weakens the connective tissue integrity and influences the thermal transformation temperature (T_s). Shrinkage temperature may be defined, therefore, as the specific point at which disruptive tendencies exceed the cohesive forces in this tissue. This temperature, thus, makes this an actual measurement of the stability of the collagen bearing tissue expressed in thermal units.

The cause of wrinkles around the eyelids, mouth and lips is multifactorial: photodamage, smoking and muscular activity such as squinting and smiling all contribute. The end result is a general loss of elasticity, which is a textural skin condition as opposed to a skin redundancy or excess of skin tissue. The surgical injection of reconstituted collagen is commonly used in order to flatten the perioral lines. While oculoplastic surgeons may treat this problem around the eye inappropriately by blepharoplasty, it has been observed that even transconjunctival blepharoplasty for removal of prolapsed retrobulbar fat fails to address the fine periocular lines or wrinkles. Until recently, the main approach to treating these blemishes has been chemical peeling by means of trichloroacetic acid or phenol. Complications of chemical peels may include hypopigmentation, scarring, cicatricial ectropion and incomplete removal of the wrinkles.

Many patients are acutely aware of these cosmetic blemishes as evidenced by the large quantity of money spent each year in the U.S. and abroad upon home and spa remedies for a more

youthful appearance. With the advent of laser technology as an alternative to chemical peels or dermabrasion, dermal ablation techniques with both the conventional carbon dioxide lasers and the high energy, short duration pulse waveform CO2 lasers, high tech solutions appear to provide substantial benefits to patients.

CO2 laser resurfacing is not a new technique. CO2 lasers have been used for several years, but regular continuous wave CO2 lasers can cause scarring due to the tissue destruction caused as heat as conducted to adjacent tissue. Even superpulse CO2 lasers produce excessive thermal damage. The Ultrapulse CO2 laser introduced by Coherent, Inc. is an attempt to assuage these drawbacks by offering a high energy, short duration pulse waveform limiting the damage to less than 50 microns allowing a char-free, layer by layer vaporization of the skin tissue.

All of the foregoing procedures depend for their success upon primary damage and the reparative potential induced by the inflammatory process in the tissue. Associated with inflammation are, of course, the four cardinal signs of inflammation of rubor (hyperemia), calor (thermal response), dolor (pain), and tumor or edema or swelling. Coincident with these manifestations is the risk of reduced resistance to infection. One must not forget that these collateral effects accompany a cosmetic enhancement procedure and, for the most part, are not associated with a therapeutic procedure. Therefore, the development of a more efficacious method would be beneficial in this regard.

With regard to joint disease and musculoskeletal complications, previous experience in the laboratory with other collagenous tissues has demonstrated the importance of understanding the mechanical response of connective tissues in terms of their hierarchical structure. The fiber morphology is reflected in the shape of the stress-strain curve.

Within the musculo-skeleton system of the human body, tendons serve as the mechanical link connecting muscle with skeleton and, thus, must possess high tensile modulus, high toughness and good resistance to tensile creep, fatigue and shock. Tendon, however, must be flexible enough to bend at joints and absorb slack when muscle tone is relaxed. This is true, also, of ligaments

which serve to connect individual bones and are important in maintaining the integrity of joint structures. It is the hierarchical organization of ligamentous and tendon collagen, as well as the annulus fibrosis component of the intervertebral disc which permit their unique qualities.

SUMMARY OF THE INVENTION

The present invention is an improved method and device for shrinking collagen. In a preferred embodiment, collagen connective tissue in skin can be contracted or shrunk instantaneously, thus tightening the overlying tissue without the superficial damage or destruction associated with other techniques of superficial skin resurfacing. In another preferred embodiment, the method and device is highly beneficial in therapeutic contraction of the collagen connective tissue within the musculo-skeletal system. These techniques match the thickness of the target tissue with the extinction depth or the spectral absorption coefficient of the specific laser wave length to gently heat the collagen molecule to the thermal shrinkage temperature, thus resulting in shrinkage of the underlying tissue while tightening the overlying skin. Superficial heat exchange either by means of passive, or more effectively, by means of a dynamic cooling process enhance this modality by eliminating pain or discomfort and reducing any risk of superficial destruction of the skin tissue.

The present invention is a method for shrinking connective collagen tissue comprising the step of irradiating the tissue with laser energy having a wavelength in the range of about 1 to about 12 microns. In a preferred embodiment, the temperature of the collagen to be shrunk is raised to between about 58 and about 62 degrees Celsius. In a preferred embodiment, the temperature of the collagen to be shrunk is raised to about 60 degrees Celsius. In a preferred embodiment, the energy has a wavelength in the range of about 1.2 to about 1.8 microns. In a preferred embodiment, the energy has a wavelength of about 1.3-1.4 microns. In a preferred embodiment, the energy is delivered in a continuous wave. In a preferred embodiment, the energy is delivered in a pulsed mode. In a preferred embodiment, the pulse rate of delivery of the laser energy is such that the

pulses of energy are delivered within the thermal relaxation time period for the given volume of tissue being thermally treated. In a preferred embodiment, the total energy delivered is in the range of about 4 to about 50 joules per square centimeter.

The present invention is a method of removing wrinkles or other tissue by shrinking the connective collagen of the target tissue comprising the step of delivering laser radiation having a thermal extinction coefficient such that the laser energy is absorbed by the target tissue below the surface of the skin. In a preferred embodiment, the laser energy is absorbed a t a depth of between about 0.01 and about 25 millimeters which corresponds to the extinction coefficient of the energy having a wavelength of between 1 and 12 microns. In a preferred embodiment, the method comprises the step of providing a heat sink on the surface of the skin to prevent significant thermal increase at the surface of the skin. In a preferred embodiment, the heat sink is a suitable laser transparent material. In a preferred embodiment, the heat sink is a suitable dynamic cooling system. In a preferred embodiment, the energy has a wavelength in the range of about 1 to about 12 microns. In a preferred embodiment, the energy has a wavelength in the range of about 1.2 to about 1.8 microns. In a preferred embodiment, the energy has a wavelength of about 1.3-1.4 microns. It has been observed that laser energy having a wavelength of between about 1.3 and 1.4 microns has an extinction coefficient of about 1.8 cm^{-1}. This corresponds to a depth of penetration of about 5.5 millimeters, the inverse of the extinction coefficient.

The present invention is a novel method for shrinking collage in joints, ligaments and musculoskeletal tissue comprising the step of irradiating the tissue with laser energy having a wavelength in the range of about 1 to about 12 microns. In a preferred embodiment, the energy has a wavelength in the range of about 1.2-1.8 microns. In a preferred embodiment, the energy has a wavelength of about 1.3-1.4 microns.

The present invention is a novel system for shrinking collagen tissue comprising a source of laser energy, the laser energy having a predetermined wavelength such that the laser energy is absorbed at a point in the tissue significantly below the surface of the skin, thereby preventing

ablation or charring of the surface tissue, and a laser delivery device, the laser delivery device capable of delivering a precise amount of laser energy to the tissue to be shrunk at a predetermined rate. In a preferred embodiment, the laser energy has a wavelength in the range of about 1 and about 12 microns. In a preferred embodiment, the laser energy has a wavelength in the range of about 1.2 and about 1.8 microns. In a preferred embodiment, the energy has a wavelength of about 1.3-1.4 microns. In a preferred embodiment, the invention further comprises a passive heat sink. In a preferred embodiment, the invention further comprises a dynamic heat sink. In a preferred embodiment, the invention further comprises a microprocessor and a controller for controlling the delivery of laser energy by the laser delivery device to the tissue. In a preferred embodiment, the invention further comprises a thermal sensing system.

Numerous other advantages and features of the present invention will become readily apparent from the following detailed description of the invention and the embodiments thereof, from the claims and from the accompanying drawings in which the details of the invention are fully and completely disclosed as a part of this specification.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a cross-section view of typical skin tissue.

FIG. 2 is a diagram showing collagen phase transition from the molecule's triple helical extra-cellular matrix native state at normal body temperature to states at the thermal shrinkage temperature wherein the collagen fibrils are both under tension and relaxed.

FIG. 3 is a schematic representation of the hierarchical structure of collagen in the tendon.

FIG. 4 is a schematic representation of the macromolecular structure of the intervertebral disc.

FIG. 5 is a graph demonstrating the temperature gradient through a portion of the skin as a function of both the wavelength of incident laser energy and the depth of laser radiation penetration.

FIG. 6 is a schematic view of a hand held temperature controlled collagen shrinkage device

used in the method of the present invention.

FIG. 7 is a graph demonstrating the temperature gradient through a portion of the skin with precooling as a function of both the wavelength of incident laser energy and the depth of laser radiation penetration.

FIG. 8 is a schematic view of a microscope mounted scanner for a temperature controlled collagen shrinkage device used in the present invention.

DETAILED DESCRIPTION OF THE INVENTION

I. COLLAGEN SHRINKAGE IN SKIN TISSUE

FIG. 1 is a cross-section view of typical skin tissue. The uppermost layer **98** of typical skin tissue is composed of dead cells which form a tough, horny protective coating. A thin outer layer, the epidermis **100** and a thicker inner layer, the dermis **102**. Intertwining S-like finger shaped portions **104** are at the interface between the epidermal papillary layer **106** and the dermal papillary layer **108**, and extend downward. Beneath the dermis is the subcutaneous tissue **110**, which often contains a significant amount of fat. It is the dermis layer which contains the major part of the connective collagen which is to be shrunk, in a preferred embodiment at an approximate target depth of between about 100 and 300 microns, according to the method of the present invention, though viable collagen connective tissue also exists to a certain degree in the lower subcutaneous layer as well. Other structures found in typical skin include hair and an associated follicle **112**, sweat or sebaceous glands and associated pores **114**, blood vessels **116** and nerves **118**. Additionally, a pigment layer **120** might be present. It will be understood that the drawing is representative of typical skin and that the collagen matrix will take different forms in different parts of the body. For example, in the eyelids and cheeks the dermis and subcutaneous layers are significantly thinner with less fat than in other areas. The target depth will be a function of the amount of scattering in the particular skin type and the associated absorption coefficient of the tissue. Furthermore, in some cases the actual target depth will correspond to one half the thickness

of the subject tissue. For example, the target depth of tissue ½ inch thick might be about ¼ inch below the surface of the skin.

FIG. 2 is a diagram showing collagen phase transition from the molecule's triple helical extra-cellular matrix native state 30 at normal body temperature to states at the thermal shrinkage temperature wherein the collagen fibrils are both under tension 32 and relaxed 34. The molecular structure of collagen in its native state is that of a triple coiled or helical crystalline protein structurally embedded within a unique ground substance. Among these unique properties are its strength and its elasticity which an analogy to nylon might be drawn. Another significant similarity with nylon is collagen's ability to undergo thermal modification resulting in the contraction or shrinking of the molecule without the substantial loss of its strength and elasticity. Within a small thermal window of 4 to 5 degrees Celsius at about 23 degrees Celsius above body temperature, the collagen molecule will undergo a contraction to 1/3 of its original length, without biochemical change. If this "thermal shrinkage temperature" (T_s) is not reached within the appropriate quantity of tissue, physical dimensional changes within the organ will either not occur or will not be sustained. If T_s is exceeded, thermal melting or denaturation of the molecule will occur with subsequent inflammation and tissue destruction, Therefore, it follows that if these conditions are satisfactorily met, the target tissue will shrink without attendant damage and destruction.

The procedure, while laser based, is basically non-destructive using the fact that normal tissue hydration acts as an universal chromophore to the wavelength of the laser. The appropriate wave length is approximately between about 1 and about 12 microns, preferably between about 1.2 and about 1.8 microns, and more preferably about 1.3-1.4 microns. This ideal wavelength depends upon the absorption of the radiation by water in order to elevate the temperature of the target tissue to T_s for collagen shrinkage - a temperature below that which results in protein denaturation.

The Nd:YAG, Nd:YAP and Nd:YALO-type lasers are such sources of coherent energy. This wavelength of 1.3-1.4 microns is absorbed relatively well by water, and as a result is attractive for tissue interaction. It is also easily transmitted through a fiber optic delivery system as

opposed to the rigid articulated arm required for the CO_2 laser. Very precise methods of controlling laser systems and optically filtering produced light currently exist. By selecting the appropriate combination of resonance optics and/or anti-reflection coatings, wavelengths in the range of 1.3-1.4 microns and even 1.32-1.34 microns can be produced.

II. COLLAGEN SHRINKAGE OF MUSCULOSKELETAL TISSUE

Many problems arise from the instability of joint structures resulting from laxity or stretching of the supporting ligamentous and capsular structures. These so-called lax ligaments frequently occur following chronic elbow, knee, and ankle injuries where a ligament has been stretched but not fractured or disrupted. Even if disruption has occurred with repair resulting from fibrosis, shortening these structures and thereby increasing their mechanical advantage without resorting to more destructive surgical intervention than endoscopic visualization and energy delivery would be of inestimable benefit

FIG. 3 is a schematic representation of the hierarchical structure of collagen in the tendon. The hierarchical organization of connective tissues is illustrated in the tendon **130**. However, virtually all connective tissues, whether soft or hard, have hierarchical structural designs arranged at discrete levels of structure. This hierarchical organization of these and other collagen bearing tissues have been widely studied and reviewed. Beginning at the molecular level with tropocollagen, progressively larger and more complex structures are built up on the nano- and microscopic scales. At the most fundamental level is the tropocollagen helix **132**. These molecules aggregate to form microfibrils **134** which, in turn, are packed into a lattice structure forming a subfibril **136**. The subfibrils are then joined to form fibrils **138** in which the characteristic structural 64-nanometer banding pattern is evident. It is these basic building blocks that, in the tendon, form a unit called a fascicle **140**. At the fascicular level the wavy nature **142** of the collagen fibrils is evident. Two or three fascicles together form the structure referred to as a tendon. It is this multi-level organization that imparts toughness to the tendon. If the tendon is subjected to excessive stresses, individual

elements at different levels of the hierarchical structure can fail independently. In this way, the elements absorb energy and protect the tendon as a whole from catastrophic failure. It is the current view that proteoglycans in association with copious amounts of water come into play as a matrix binding the fibrils together. Proceeding toward macroscopic dimensions, the fascicles comprising crimped collagen fibrils are embedded in the proteoglycan-water gel with several fascicles in turn making up the functioning tendon or ligament.

FIG. 4 is a schematic representation of the macromolecular structure of the intervertebral disc **150**. In a stacked configuration, intervertebral discs are interspersed between the vertebral bones in the spinal column. One of the functions of the discs is to absorb compressive forces or loads placed on the spine and skeletal structure while moving or performing functions. It was recently shown that the annulus fibrosis **152**, the outer component of the intervertebral disc that is made up of discrete layers or lamellae **154** of fibrous collagen arrayed around the nucleus like the layers of an onion skin. The hierarchical structure with gradient characteristics at the various levels of organization is not unlike that of tendon or ligamentous tissues. In the intervertebral disc, the collagen fibrils organized into lamellar sheets in the annulus fibrosus surround a gelatinous and highly hydrated nucleus pulposis **156**. The thickness of lamellae vary with location and are thicker at the anterior and lateral aspects of the disc than at the posterior. With lamellae, fibrils are parallel and inclined with respect to the axis of the spinal column by an interlamellar angle A which alternates in successive lamellae. This angle decreases from the edge of the disc inward. At higher magnification, the fibrils have a planar zig-zag waveform. The crimp angle B is largest in fibrils close into the nucleus and decreases toward the periphery. The orientation of the collagen fibrils in the annulus gives the disc strength and stability in tension, bending, and torsional motions. Based upon optical microscope observations of the morphology of the collagen fibrils, the levels of structural hierarch below the fibrils are assumed to be identical to that of the tendon and intestine. Axial compression, in addition to torsion and bending, is a mode of deformation normally experienced by the disc. It is generally believed that compressive forces are transmitted across the

disc to the fibers of the outer lamellae, which are held in tension. Although the nucleus is thought to play a major role in the transmission of forces, the restoring force of the stretched fibers of the annulus is considered to balance the effects of nuclear pressure. The fibers of the lamellae are constrained at the cartilage end-plates of the vertebral bodies, so they must extend in length to accommodate the bulging. Even though the disc undergoes macroscopic compression, the fibers of the lamellae are loaded in tension and their mode of deformation can be compared with other connective tissues such as tendon and intestine.

This type of tissue belongs to the family of uniaxial composites. The significant aspect of a composite is its unique set of mechanical properties. This is achieved through the synergistic mechanical interplay between structural elements.

When tendon or ligament is deformed beyond its elastic limit, permanent elongation occurs. Individual elongated collagen fibrils have been observed. Elongations of up to 900% have been reported. The fibril banding was proportionately extended, though above 200% extension when observed during experimental conditions, certain band regions extended slightly more than others under electron microscopy.

Small angle x-ray diffraction patterns revealed that even though there is definite crystallographic damage within the collagen fibrils, they are still entirely capable of bearing load. To impart tensile strength in the collagen fibril, which is constructed of discrete structural units, the tropocollagen macromolecules, some type of lateral bonding force is required where tropocollagen units overlap. The slippage mechanism by which a collagen fibril elongates involves slippage of the tropocollagen units within the microfibril. This requires over coming the lateral bonding forces but does not result in these forces being completely and permanently destroyed. Load bearing ability is maintained, or even improved, when intrafibrillar strain hardening occurs. Although it is evident that the principal deformation events take place within the collagen molecule, the mucopolysaccharide matrix plays a secondary role. The most obvious mechanical function of the matrix is to bind the collagen fibrils into a functional sliding cord. This matrix, which is more

currently characterized as glycosaminoglycan or GAG, serves to cement the fibers together into fiber bundles and provides the lateral bonding force required for load bearing.

Evidence exists to elevate the mechanical role played by the GAGs in the tendon as it does in other collagen bearing tissues. Removing this matrix by enzymes or other reagents as disclosed in U.S. Patent No. 5,304,169, considerably weakens the connective tissue and influences the thermal transformation temperature or shrinkage temperature. Shrinkage temperature, therefore, in certain instances and mechanisms of collagen shrinkage in the human body, may be defined as the specific point at which disruptive tendencies exceed the cohesive forces in the tissue. This temperature thus makes this an actual measurement of the stability of the collagen bearing tissue expressed in thermal units.

In the traditional treatment of disc prolapse, or herniated intervertebral disc, the disc is removed surgically although, paradoxically, the pathological process resides in the annulus fibrosis and not in the disc. It is, in fact, a disruption in the annulus, usually in the posterior-lateral aspect, which secondarily results in bulging of the disc. Herniation and finally extrusion of a fragment of the disc is the ultimate result. At the level of the disc bulge and herniation, shrinkage of the stretched collagenous annulus fibrosis would be the procedure of choice. The appropriate approach for this intervention would be by means of direct myeloscopy or percutaneous endoscopy in order to shrink this tissue and thus contain the nucleus pulposis. Exposing the weakened annulus to the mid-infrared laser energy while retracting the nerve root would avoid violation of the disc and creation of segmental instability.

Additional specific examples of the benefit of the use of mid-infrared laser energy within the spectra absorption or extinction coefficient range of 0.4 cm^{-1} - 1000 cm^{-1}, corresponding to the wavelength range within the electromagnetic spectrum of 1.0 microns to 12.0 microns for the shrinkage of collagen connective tissues are as follows: shrinkage of the medial or lateral collateral , or the anterior cruciate ligament of the unstable knee joint and the treatment of the chronic unidirectional and multidirectional glenohumeral instability or tightening of the shoulder capsule in

recurrent dislocation.

III. OPTIMUM WAVELENGTH: 1.3-1.4 MICRONS

FIG. 5 is a graph demonstrating the temperature gradient through a portion of the skin as a function of both the wavelength of incident laser energy and the depth of laser radiation penetration. No external cooling is used. The graph demonstrates a change in temperature (ΔT) of about 60 degrees Celsius and all curves are shown for the time point 1 millisecond following exposure to the laser energy. The graph shows three lines corresponding to laser wavelengths of 10.6 microns, 1.3-1.4 microns and 1.06 microns.

The present invention utilizes laser energy having a wavelength between about 1 and about 12 microns, more preferably between about 1.2 and about 1.8 microns, and more preferably about 1.3-1.4 microns. This type of laser energy is most frequently produced by a Nd:YAG, Nd:YAP or Nd:YALO-type laser. A laser operating at these wavelengths may either have a high repetition pulse rate or operate in a continuous wave mode. This laser has been investigated in the medical community as a general surgical and tissue welding device, but has not been used for collagen tissue shrinkage in the past. Indeed, the prior art teaches away from the use of laser energy at 1.3-1.4 microns for shrinking human collagen.

As early as 1989, studies related to tissue fusion have been performed with lasers operating at 1.3-1.4 microns. The use of laser radiation at this wavelength for shrinking collagen in any application is heretofore essentially unknown. One author discloses results to prove efficacy of such a laser in rupturing secondary membranes after extracapsular surgery. Others have disclosed the use of the 1.3-1.4 micron laser for the treatment of rectosigmoideal tumors. Numerous tissue welding applications of the 1.3-1.4 micron laser such as wound healing, cosmetic skin closure, vascular surgery and minimally invasive surgical procedures normally performed with resorbable and removable sutures or staples have also been studied. However, these surgical procedures including incision, excision, ablation and cauterization of tissue are essentially disruptive processes.

IV. HEAT SINK METHODOLOGY

Studies have shown that the CW laser with an appropriate heat sink produced a more optimum thermal profile for collagen shrinkage. It has been shown that irradiating tissue with a midinfrared laser source through a surface thermal absorption element or heat sink permits an optimum thermal profile within the target tissue with near physiologic temperature at the surface of the irradiated surface thus minimizing surface thermal damage. In the case of desired thermal collagen shrinkage, this is clearly the desired condition. Attenuating the surface temperature before laser irradiation and therefore creating a boundary layer on the skin surface can result in selective cooling of the target tissue thus preserving the normal overlying epidermis.

Providing a glass or sapphire tip probe to the surface of the tissue being lased, while transparent to the laser radiation being delivered to the tissue, will act as an efficient and convenient heat sink for the surface layers of the skin.

FIG. 6 is a schematic view of a hand held temperature controlled collagen shrinkage device used in the method of the present invention. Modern instruments to provide dynamic cooling of the surface layers of tissue are well suited to these applications. A typical handpiece 40 comprises the laser delivery device as well as various peripheral systems. A fiber optic cable 42 guides the laser light into the device. A preferred embodiment of such a device contains a focusing lens 44 and, optionally, other laser optics or mechanical equipment including a beam splitter, focusing knob and adjustable mounting means, thereby producing a laser focus spot 46 on the surface of the tissue above the collagen to be shrunk. If the laser source does not have a fiber tip thermal protection system to monitor the surface temperature as well as to prevent thermal runaway in certain situations, a separate electronic or other thermal detector 48 is useful. Additionally a coolant spray 50 can be provided through the handpiece or it could be provided with another separate device. Finally, a connection to a computer and the laser 52 will allow the device to utilize the electronic or other thermal sensing means and obtain feedback control signals for the handpiece. With respect to studies performed removing sub-dermal skin lesions, such as port wine stains and other red or

brown marks, an optimum cooling strategy might be one that uses a short spurt of cryogen (e.g., 5-20 ms) to reduce the local temperature in the pigmented epidermis, while minimizing attenuation of the laser light by the boundary layer, followed by post-irradiation cooling spurt that provides a heat sink for dissipation of the epidermal heat generated by melanin absorption. An appropriate cryogen spray would be tetrafluoroethane, $C_2H_2F_4$, an environmentally compatible, non-toxic, non-flammable freon substitute. In clinical application the distance between the aperture of the spray valve and the skin surface should be maintained at about 20 millimeters.

During a typical dynamic cooling process, the surface of the skin is pre-cooled to as low as 0 degrees Celsius or lower, at a rate fast enough to cool the surface only but not dissipate heat from below about 400-500 microns below the surface. In a preferred embodiment, during the cooling step the target tissue remains at body temperature and is not cooled at all. By applying cooling to the surface of the skin for a short period of time, typically between about 5 and 100 milliseconds and then delivering laser energy, the surface is initially cooled but the target tissue never is. Generally, the surface layer of skin is rapidly cooled. A high rate of cooling will prevent local and vicinal hypothermia and will also tend to have a numbing, anesthetic or analgesic effect. It will be understood that in at least one preferred embodiment of the method of the present invention, since only a relatively very thin outer layer of skin is cooled in a relatively very rapid period of time, laser energy must be applied either contemporaneously with or immediately after termination of passive or dynamic cooling. Therefore, upon delivery of laser energy onto the surface and therethrough, the target tissue will be raised to the optimal thermal shrinkage temperature and generally not any higher, in an adequately rapid process, with the surface temperature of the skin remaining unelevated from body temperature, or if elevated at all, not elevated to a temperature which would have any adverse effect on the tissue. Adverse effects of elevated tissue surface temperature include discomfort or pain, thermal denaturing of proteins and necrosis of individual cells at the surface. In a preferred embodiment of the method of the present invention, cooling and heating are performed in a predetermined timing sequence, optionally with the use of timer circuits

and/or other controller means.

Thus, it will be obvious to those skilled in the art that a passive heat sink includes glass or sapphire tip probes, and other types of devices to lay on the surface of the skin. It will also be obvious that a dynamic type of heat sink will refer to those actively cooled by flowing gas or liquid, jets or spurts of coolant such as freon, and other active types of heat exchangers suitable for surface cooling while irradiating sub-surface portions of collagen tissue.

FIG. 7 is a graph demonstrating the temperature gradient through a portion of the skin with precooling as a function of both the wavelength of incident laser energy and the depth of laser radiation penetration. The graph demonstrates a change in temperature (ΔT) of about 60 degrees Celsius. In these experiments, precooling of the skin surface tissue for a period of 20 milliseconds was conducted immediately prior to exposure to laser energy. All curves are shown for a time point 1 millisecond following exposure to the laser energy. The graph shows three lines corresponding to laser wavelengths of 10.6 microns, 1.3-1.4 microns and 1.06 microns.

V. SCANNING AND THERMAL SENSING METHODOLOGY

Scanners such as those manufactured by Sharplan and Reliant Technologies are presently available. These devices utilize one or more rotating mirrors to scan the beam over a circular or other shaped area. Power density of the beam incident on the tissue can be adjusted manually or by computer control. Automatically scanned systems previously used to vaporize holes into tissue with complex shapes and precisely defined dimensions, can be used in collagen shrinking applications as well. Applications where large areas of tissue are to be irradiated with a certain predetermined spectrum or gradient of power density over those areas are particularly well suited for computer-controlled laser scanner systems.

By combining an electronic thermal sensing and feedback loop in the application probe and, optionally, precooling the tissue by means of a freon spray, the physician has exquisite control over the thermal shrinking modality in his hand. The electronic thermal sensor can be a fast

response thermocouple like the OS40 series devices from Omega. This detector will analyze a 0.125 inch spot from 1" away and accurately indicate temperature within 0.1 seconds, fast enough to servo the applied laser energy or to simply turn it off when the desired temperature has been reached.

In addition to precooling tissue, the safe and appropriate application of the laser energy requires accurate delivery of the laser energy to the target tissue. The laser energy can be delivered in a continuous or pulsed wave by means of a highly accurate fiber optic microprocessor controlled delivery system known. Various devices are currently being sold for such applications. A coherent energy source with the efficiency of a smaller physical foot-print avoiding the cryogenic cooling and energy requirements of the laser, itself, would be the solid state 1.2-1.8 micron emitting laser diode (which can be precisely tuned across almost it's entire range of possible wavelengths). The integration of an aiming beam such as that provided by a He:Ne laser, or more effectively from a visible light emitting diode, would complete the package.

FIG. 8 is a schematic view of a microscope mounted scanner for a temperature controlled collagen shrinkage device used in the present invention. In this view, a laser console 60 is installed adjacent a floor-mounted microscope 62. A fiber optic cable 64 conducts laser energy from the laser source to the scanner 66. A laser delivery attachment 68 may be necessary to conduct the laser energy in an appropriate beam pattern and focus. In this embodiment of the invention, servo feedback 70 signals are also conducted along the fiber optic back to the laser console. The servo feedback signals could also be directed back to the laser console via an additional fiber optic or other wiring or cabling. This servo feedback may comprise thermal or optical data obtained via exter...i sensors or via internal systems, such as a fiber-tip protection system which attenuates the laser energy transmitted, to provide control in operation and to prevent thermal runaway in the laser delivery device. Thus, a thermal feedback controller 72 will regulate the laser energy being transmitted. This controller can comprise an analog or digital PI, PD or PID-type controller, a microprocessor and set of operating instructions, or any other controller known to those skilled in

the art. Other preferred embodiments can also be provided with additional features. For example, the surgeon or technician operating the laser could also manipulate an energy adjust knob 74, a calibration knob 76 and a footpedal 78. Thus, in a preferred embodiment, a very accurately adjustable system is provided which allows a surgeon to deliver laser energy via a computer controlled scanning device, according to instructions given by the surgeon or an observer inspecting the region of the skin where collagen is to be shrunk through a very accurate microscope. Once a region to be treated is located, the scanner can deliver a very precise, predetermined amount of laser energy, in precisely chosen, predetermined regions of the skin over specific, predetermined periods of time.

It will be understood that, while the procedures described herein may vary slightly in the equipment required, their energy transmission rates, times, powers and other factors, the above described parameters can be adapted easily to perform a great number of operations, more efficiently and more safely than before. Another modification to the procedure will be the adaptation of the procedure to photodynamic therapies (PDT). The tissue of interest can be infused with a photoactive agent prior to delivery of laser energy thereto.

While the principles of this invention have been made clear in illustrative embodiments, there will be immediately obvious to those skilled in the art many modifications of structure, arrangement, proportions, the elements, materials, and components used in the practice of the invention, and otherwise, which are particularly adapted to specific environments and operative requirements without departing from those principles. The appended claims are intended to cover and embrace any and all such modifications, within the limits only of the true spirit and scope of the invention.

We claim:

1. A method for shrinking collagen tissue by irradiation of the target collagen tissue with laser energy to increase the temperature of the target collagen tissue and induce thermal contraction thereof, the method comprising the following steps:

(a) providing a laser source with laser energy having a wavelength in the range of about 1 to about 12 microns and providing a suitable laser energy delivery device;

(b) positioning the delivery device adjacent the skin layer covering the collagen tissue to be shrunk, the skin layer being essentially at ambient body temperature and the target collagen tissue being in it's native state;

(c) delivering a predetermined amount of laser energy to the collagen tissue via the delivery device so as to cause the temperature of a given volume of the target collagen tissue to rise to a predetermined temperature, the laser energy delivered to the collagen tissue in a controlled and predetermined intensity and rate, thereby inducing the target collagen tissue to undergo thermal phase transition from it's native state to a state wherein the collagen tissue has begun to contract and the tissue is under tension by the stress induced thereby; and

(d) allowing the temperature of the target collagen tissue to return to it's ambient temperature or close thereto, thus achieving a shrinkage of the target collagen tissue now contracted to a physical dimension significantly smaller than that of it's native state.

2. The method of claim 1 wherein the temperature of the target collagen tissue is raised to between about 58 and about 62 degrees Celsius during step (c).

3. The method of claim 1 wherein the temperature of the target collagen tissue is raised to about 60 degrees Celsius during step (c).

4. The method of claim 1 wherein the laser energy delivered during step (c) has a wavelength in the range of about 1.2 to about 1.8 microns.

5. The method of claim 1 wherein the laser energy delivered during step (c) has a wavelength of about 1.3-1.4 microns.

6. The method of claim 1 wherein the laser energy delivered during step (c) is delivered in a continuous wave.

7. The method of claim 1 wherein the laser energy delivered during step (c) is delivered in a pulsed mode.

8. The method of claim 7 wherein the pulse rate of delivery of the laser energy delivered during step (c) is such that the pulses of energy are delivered within the thermal relaxation time period for the given volume of tissue being thermally treated.

9. The method of claim 1 wherein the total energy delivered to the target tissue is in the range of about 4 to about 50 joules per square centimeter.

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10. A method for removing wrinkles and shrinking target facial and body tissue comprising collagen by irradiation of the collagen tissue with a suitable type of laser energy, the laser energy having a thermal extinction coefficient such that the laser energy is absorbed by the target tissue below the surface of the skin, in order to increase the temperature of the target collagen tissue and induce thermal contraction thereof, the method comprising the following steps:

(a) providing a laser source with laser energy having a wavelength in the range of about 1 to about 12 microns and providing a suitable laser energy delivery device;

(b) positioning the delivery device adjacent the wrinkled or excess skin layer covering the collagen tissue to be shrunk, the skin layer being essentially at ambient body temperature and the target collagen tissue being in it`s native state;

(c) delivering a predetermined amount of laser energy to the collagen tissue via the delivery device so as to cause the temperature of the target collagen tissue to rise to a predetermined temperature, the laser energy delivered to the collagen tissue in a controlled and predetermined intensity and rate, thereby inducing the target collagen tissue to undergo thermal phase transition from it`s native state to a state wherein the collagen tissue has begun to contract and the tissue is under tension by the stress induced thereby; and

(d) allowing the temperature of the target collagen tissue to return to it`s ambient temperature or close thereto, thus achieving a shrinkage of the target collagen tissue now contracted and condensed to a physical dimension significantly smaller than that of the native state and producing a tighter skin surface which contains a greater amount of internal tension and stretch than initially.

11. The method of claim 10 wherein the laser energy delivered during step (c) is absorbed by the collagen tissue below the wrinkled or excess skin surface at a depth of between about 0.01 and about 25 millimeters.

12. The method of claim 10 further comprising the following step (b-1) between steps (b) and (c):

(b-1) providing a heat sink on the surface of the skin to prevent significant temperature increase of the wrinkled or excess skin.

13. The method of claim 12 wherein the heat sink is a suitable, laser transparent material.

14. The method of claim 12 wherein the heat sink is a suitable, dynamic cooling system.

15. The method of claim 10 wherein the energy has a wavelength in the range of about 1 to about 12 microns.

16. The method of claim 10 wherein the laser energy delivered during step (c) has a wavelength in the range of about 1.2 to about 1.8 microns.

17. The method of claim 10 wherein the laser energy delivered during step (c) has a wavelength of about 1.3-1.4 microns.

18. A method for shrinking collage in joints, ligaments and musculoskeletal tissue comprising the step of irradiating the tissue with laser energy having a wavelength in the range of about 1 to about 12 microns.

19. The method of claim 18 wherein the energy has a wavelength in the range of about 1.2-1.8 microns.

20. The method of claim 18 wherein the energy has a wavelength of about 1.3-1.4 microns.

21. A method for the treatment of a prolapsed intervertebral disc, a prolapsed or herniated disc being one in which a portion of the inner nucleus pulposis bulges out into or through a part of the annulus fibrosis, the method comprising the following steps:

(a) providing a laser source with laser energy having a wavelength in the range of about 1 to about 12 microns and providing a suitable laser energy delivery device;

(b) positioning the delivery device adjacent the prolapsed intervertebral disc; and

(c) delivering a predetermined amount of laser energy to the annulus fibrosis to contain the prolapsed portion of the nucleus pulposis.

22. A device for shrinking collagen tissue comprising:

a source of laser energy, the laser energy having a predetermined wavelength such that the laser energy is absorbed at a point in the tissue significantly below the surface of the skin, thereby preventing ablation or charring of the surface tissue;

a cooling means, the cooling means for cooling the surface of the skin prior to delivery of laser energy thereto; and

a laser delivery device, the laser delivery device capable of delivering a precise amount of laser energy to the tissue to be shrunk at a predetermined rate.

23. The device of claim 22 wherein the laser energy has a wavelength in the range of about 1 and about 12 microns.

24. The device of claim 22 wherein the laser energy has a wavelength in the range of about 1.2 and about 1.8 microns.

25. The device of claim 22 wherein the energy has a wavelength of about 1.3-1.4 microns.

26. The device of claim 22 further comprising a passive heat sink.

27. The device of claim 22 further comprising a dynamic heat sink.

28. The device of claim 22 further comprising a microprocessor and a controller for controlling the delivery of laser energy by the laser delivery device to the tissue.

29. The device of claim 22 further comprising a thermal sensor and means for thermal feedback.

30. The device of claim 22 further comprising a scanning device to irradiate a predetermined area of skin.

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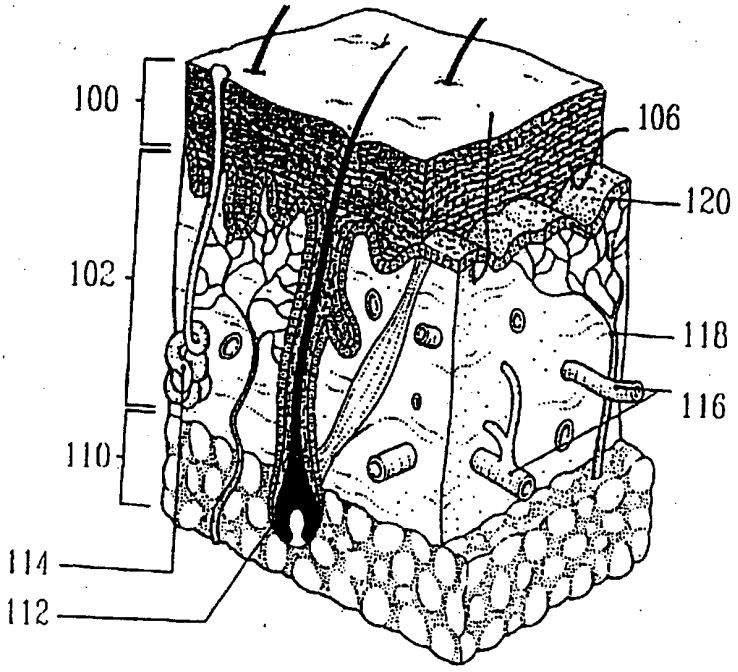


FIGURE 1

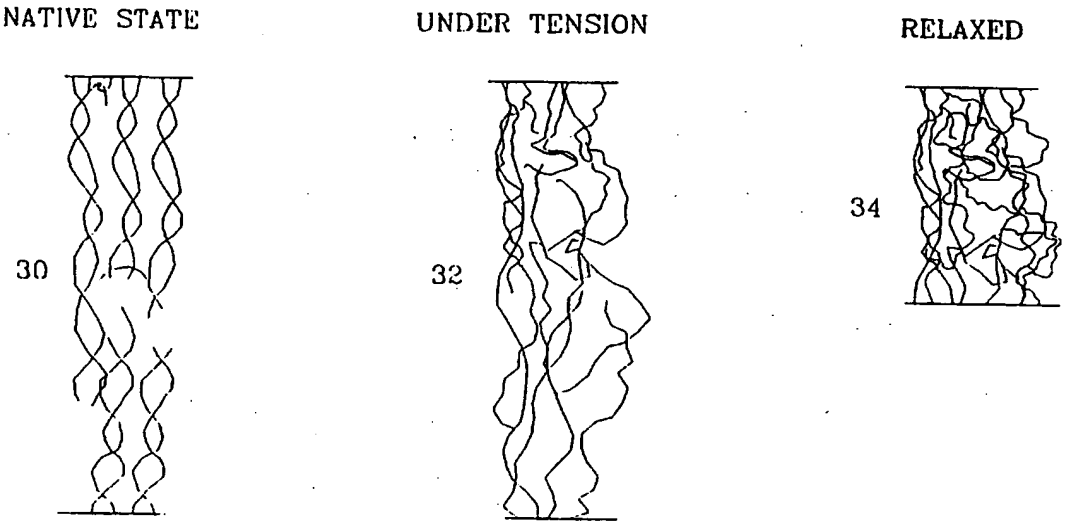


FIG. 2

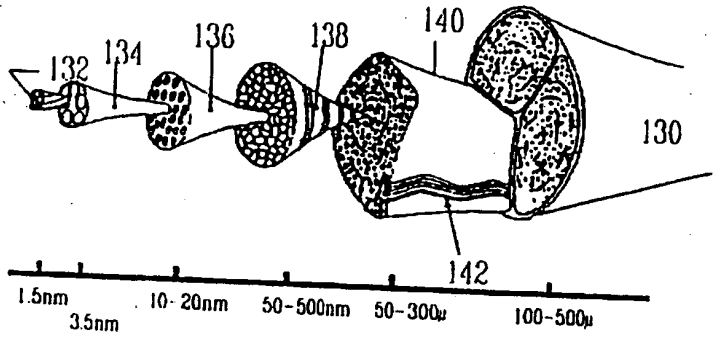


FIGURE 3

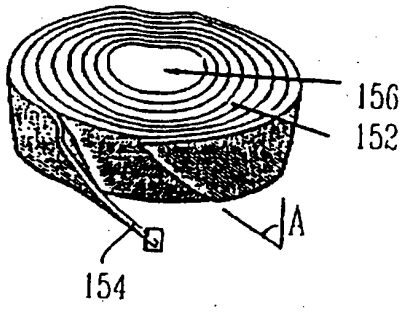


FIGURE 4A

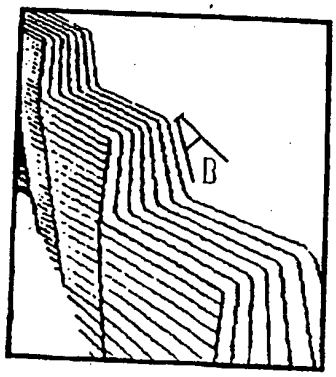
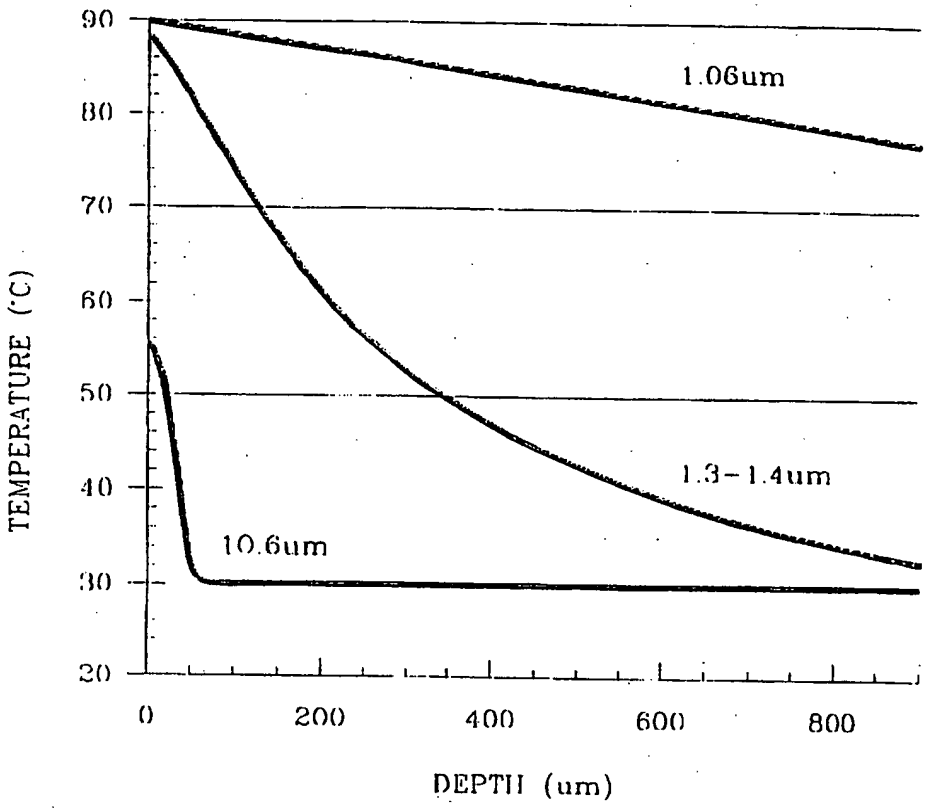


FIGURE 4B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60
50
40
30
20
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1.3-1.4um
10.6um
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200
400
600
800
DEPTH (um)

FIG. 5

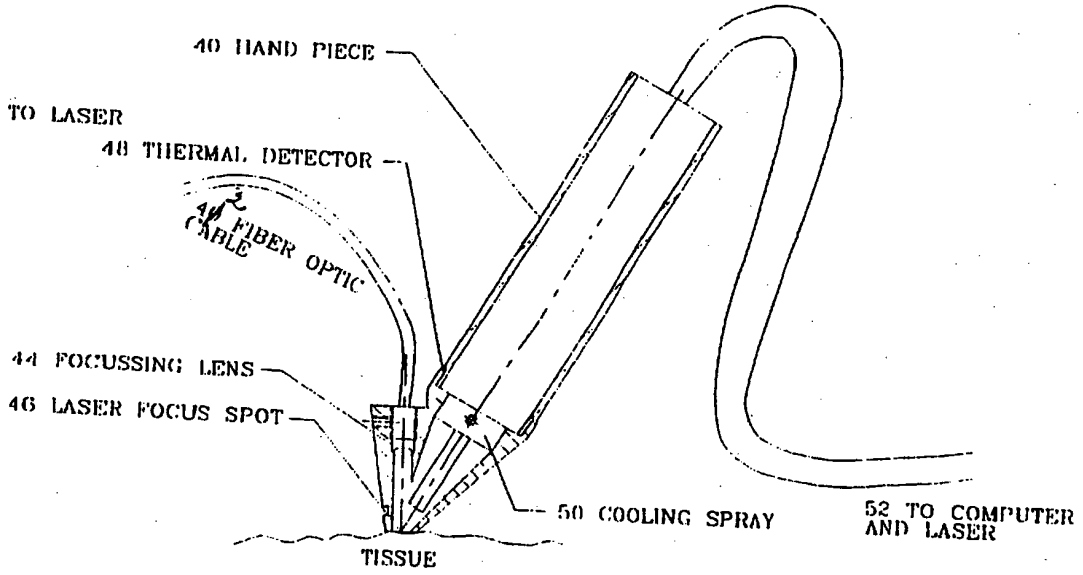
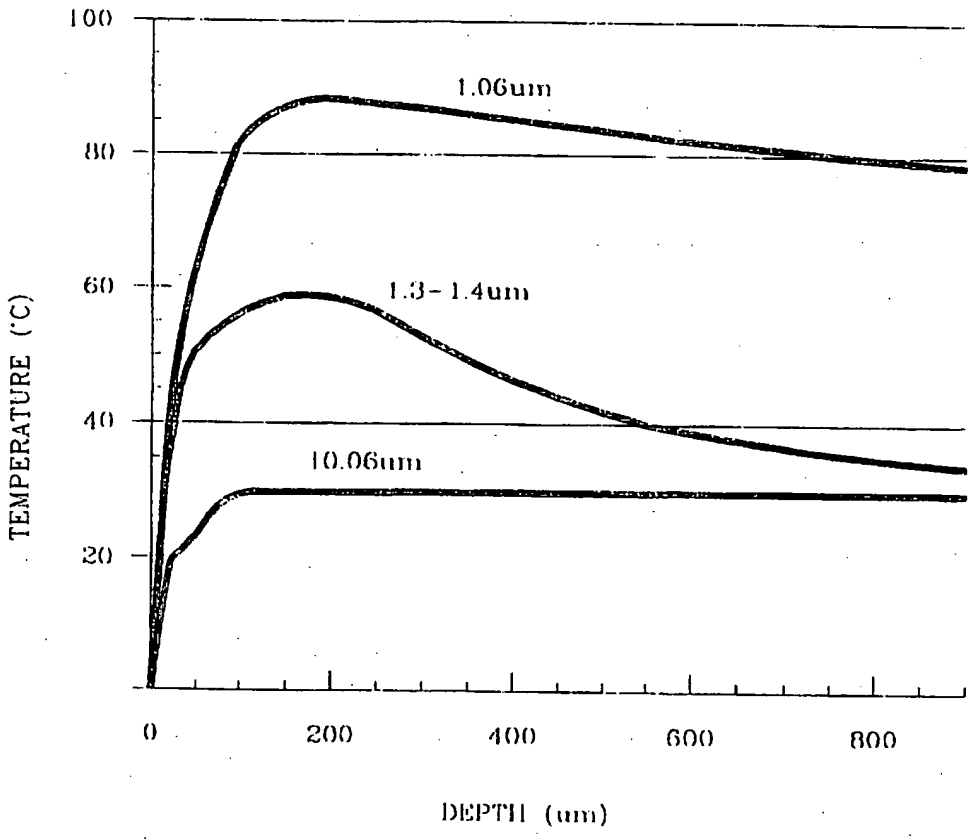

40 HAND PIECE
TO LASER
48 THERMAL DETECTOR
42 FIBER OPTIC CABLE
44 FOCUSSING LENS
46 LASER FOCUS SPOT
50 COOLING SPRAY
52 TO COMPUTER AND LASER
TISSUE

FIG. 6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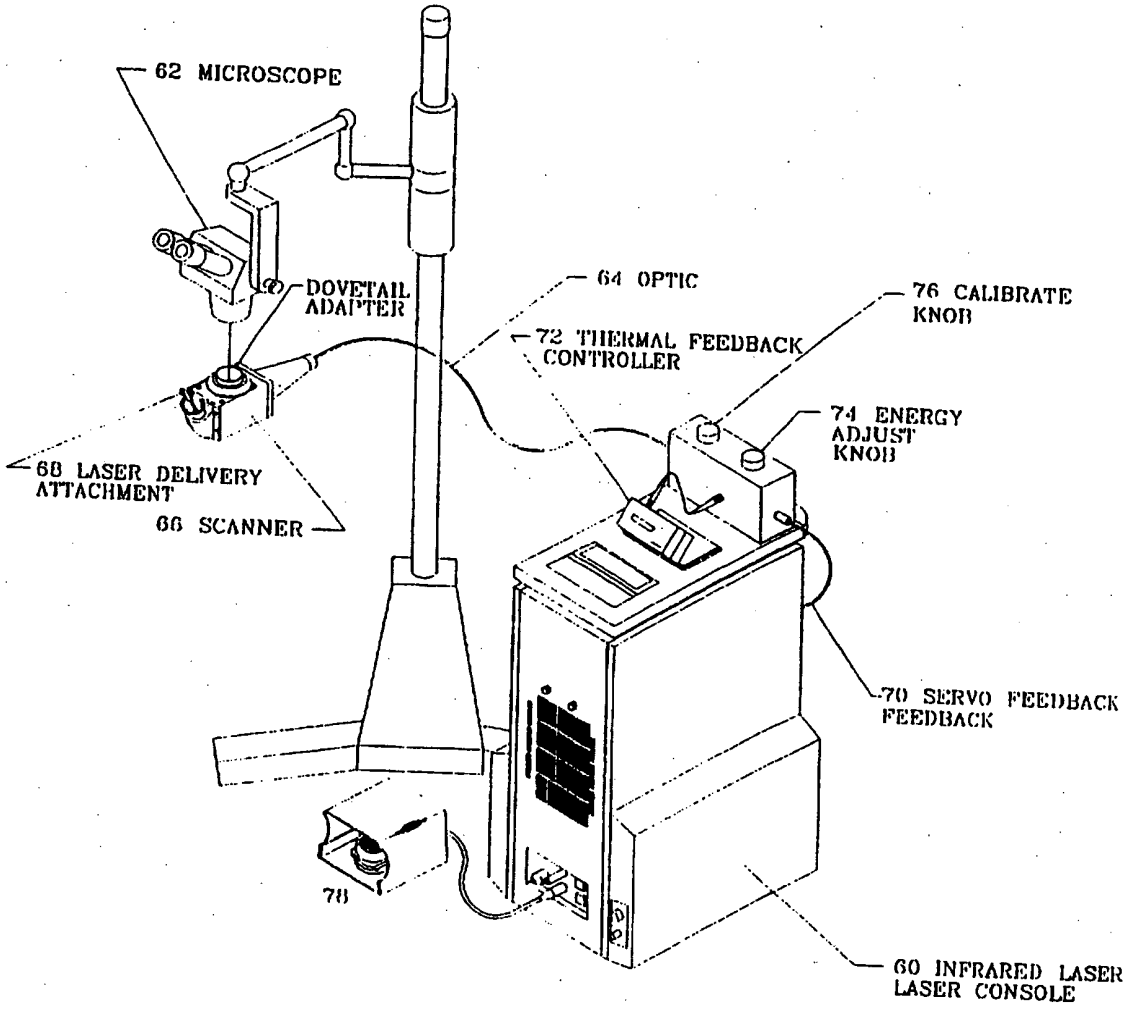
DEPTH (um)

FIG. 7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DOVETAIL ADAPTER
64 OPTIC
72 THERMAL FEEDBACK CONTROLLER
76 CALIBRATE KNOB
74 ENERGY ADJUST KNOB
68 LASER DELIVERY ATTACHMENT
66 SCANNER
70 SERVO FEEDBACK FEEDBACK
78
60 INFRARED LASER LASER CONSOLE

FIG. 8

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/03449

A. CLASSIFICATION OF SUBJECT MATTER
IPC(6) :A61N 5/06
US CL :606/009
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 606/8-17

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 4,976,709 A (SAND) 11 December 1990, entire document.	1-10, 12-16, 18 19, 21-24, 26-28 --- 11, 17, 20, 25, 29
Y	US 5,334,191 A (POPPAS et al.) 02 August 1994, entire document.	29
A	US 4,854,320 A (DEW et al.) 08 August 1989, entire document.	1-29
A	US 5,071,417 A (SINOFSKY) 11 December 1991, entire document.	1-29

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 19 MAY 1997	Date of mailing of the international search report 09 JUN 1997
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer SONYA HARRIS Telephone No. (703) 308-0858